Non-Technical Abstract

In animal models, regression of several types of tumors following administration of recombinant IL-2 protein (Interleukin 2) or adenoviral vectors expressing IL-2 has been reported. IL-2 is effective because it promotes an anti-tumor immune response.

The purpose of this clinical study is to study a non-viral gene therapy that produces IL-2. It is anticipated that this product will promote tumor regression or inhibition of progression of squamous cell carcinoma of the head and neck. Data from rodent tumor models support this hypothesis. Intratumoral administration of the IL-2 Gene Medicine results in an increase in the levels of IL-12 and γ-IFN, two cytokines that are known to contribute to an anti-tumor immune response. When administered intratumorally to tumor-bearing mice, IL-2 Gene Medicine slows tumor growth. These data suggest that administration of the formulated hIL-2 plasmid also will lead to the generation of an anti-tumor immune response and subsequent tumor regression, inhibition in tumor progression, and/or prevention of metastasis in humans.

The ability of recombinant IL-2 protein to induce an anti-tumor immune response is documented. However, in order to achieve effective levels of IL-2 in the tumor, high doses of the recombinant protein have been administered intravenously. These high doses of recombinant protein have serious side-effects. The proposed project is directed at expressing human IL-2 in the tumor by liposome-mediated delivery of a therapeutic gene encoding IL-2. This gene therapy will induce local (tumoral) expression of IL-2 to induce an anti-tumor response without producing high concentrations of IL-2 throughout the body. This offers a distinct advantage since the likelihood of occurrence of side-effects from high doses of IL-2 should be greatly reduced, if not eliminated. In addition, the IL-2 protein lasts in the blood for only 6-10 minutes, thereby requiring multiple administrations for optimal effect. IL-2 gene therapy is expected to produce protein in the tumor for days, obviating the need for multiple administrations. Finally, liposome-mediated DNA delivery does not utilize a recombinant virus for delivery of the therapeutic gene, thereby eliminating potential side-effects associated with virus exposure.

A Phase I trial in patients with head and neck cancer has been completed. This study was designed to evaluate safety, and showed that single and multiple intratumoral injections of IL-2 Gene Medicine were safe and well-tolerated. The current study is designed to evaluate the clinical efficacy and safety of IL-2 Gene Medicine in patients with the same condition, and will be compared to treatment with a standard chemotherapy (methotrexate). Each patient will receive multiple (up to 14) intratumoral injection of formulated IL-2 plasmid over a 12-week period, or methotrexate following standard and approved procedures. Physical examinations and evaluations of clinical chemistry and hematology will be conducted to assess safety and tolerability. In addition, nucleic acid (RNA) studies will be performed with tissue obtained by biopsy to evaluate expression of the IL-2 transgene. Clinical efficacy will be evaluated by clinical and radiological measurements of tumor size, and measurements of survival, time to disease progression, and quality of life.